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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/615,624	07/13/2000	Peter C. Brooks	13761-734	3563

26021 7590 12/23/2003

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EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/615,624	BROOKS ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-106* is/are pending in the application.

4a) Of the above claim(s) *18-21 and 25-104* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17, 22-24, 105-106* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

The Amendment filed September 8, 2003 in response to the mailing of a Notice of a Non-compliant Amendment (August 18, 2003) is acknowledged and has been entered. It is further noted that this Office Action addresses the *arguments* presented in Paper No. 19 filed August 11, 2003 since applicants did not provide any additional arguments with the presently entered amendment of September 8, 2003.

Claims 105 and 106 were added.

Claims 18-21, and 25-104 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 1-17, 22-24, and 105-106 are pending and are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Drawings

The drawings are no longer objected to because Applicants have submitted (Paper No. 19) that the color photographs in Figures 6A and 6B were submitted for examination purposes only.

Rejections Maintained:

The specification AND claims **15-16** remain rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure for the reasons of record in the action mailed 02-11-03, pages 4-5. Applicant's assurances that an acceptable deposit of the hybridoma producing the claimed antibody will be made before the date of payment of the issue fee is not persuasive to remove the rejection from the record because the as-filed application is not presently in condition for allowance. See MPEP 37 CFR 1.809(c).

Claims 1-14, 17, 22-24 remain rejected and new claims 105-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over MELVIN *et al.* (WO 97/00449, January 1997) in combination with the teachings of Newton *et al.* (Int'l. Jnl. Oncol., Vol. 6, pages 1063-1070, 1995) for the reasons of record in the Action mailed 02-11-03, pages 10-11.

Applicants argue (Paper No. 19, page 7) that Melvin and Newton, when considered "separately", do not teach or suggest the instant claim 1. This argument has been considered but cannot be found persuasive because one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) MPEP 2145.

Applicants further argue (page 8) that the antagonists of the present invention are not a simple mixture of two known antagonists, but novel chemical entities. As an example, Applicants point to the specification which "describes antagonists of the present invention" such as the synthetic peptide FRIP-9 and the antibody FM155. Applicants further argue that a

mechanical mixing of the antagonists of Melvin and Newton as suggested would not have resulted in new chemical entities of the present invention, such as the peptide FRIP-9 and the antibody FM155. This argument has been considered but is not found persuasive because arguments that rely on a particular distinguishing features are not persuasive when those features are not recited in the claims. Narrow limitation contained in the specification cannot be inferred in the claims where the elements not set forth in the claims are linchpin of patentability. See In re Philips Industries, Inc. v. State Stove & Mfg. Co., 522 F.2d 1137, 186 USPQ 458 (CA6 1975), 237 PTJA A-12. While the claims are to be interpreted in light of the specification, it does not follow that limitations from the specification may be read into claims. On the contrary, claims must be interpreted as broadly as their terms reasonably allow. See Ex parte Oetiker, 23 USPQ2d 1641 (BPAI, 1992). Applicant is reminded that the claims *define* the subject matter of his invention and that the specification cannot be relied upon to read limitations into the claims.

Applicants further argue (page 9) that nothing in the recited art suggests antagonists that inhibit angiogenesis and or tumor growth by modifying interactions between proteolytic enzymes and integrins. This argument has been considered but is not found persuasive. As set forth previously, Melvin anticipates antagonists that directly inhibit the activity of proteolytic enzymes (e.g. MMP-9) which can be used to inhibit a diseased state such as cancer. Likewise, Newton teaches antagonists of integrins that are useful for inhibiting metastasis of tumor cells. Thus, the prior art clearly suggests and or teaches antagonists that modify the interactions between proteolytic enzymes and integrins. Thus, it appears that Applicant has argued and discussed the references individually without clearly addressing the combined teachings. It must be remembered that the references are relied upon in combination and are not meant to be

considered separately as in a vacuum. It is the combination of all of the cited and relied upon references which made up the state of the art with regard to the claimed invention. Furthermore, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and it is not that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

New Rejections:

Claims 1-14, 16-17, 22-24, and 105-106 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth an antagonist that inhibits the interaction between MMP-9 and $\alpha 5\beta 1$ integrin wherein said antagonist is the polypeptide of SEQ ID NO:1 or the monoclonal antibody FM155. Thus, the written description is not commensurate in scope with the claims drawn to a genus of antagonists that modify protein-protein interactions between any proteolytic enzyme and any integrin.

The specification teaches (page 9) that antagonists of the invention may be any type of molecule, thus applicants' claims encompass a genus of antagonists with the stated biological

properties. However, the written description only reasonably conveys the peptide FRIP-1 (SEQ ID NO:1) and a monoclonal antibody (FM155) that binds to said peptide. The instant disclosure of a single species of a peptide and an antibody that binds to said peptide fails to adequately describe the scope of the claimed genus (any antagonist), which encompasses a substantial variety of subgenera-, i.e. peptides, organic molecules, enzymes, antibodies, or oligonucleotides (page 9, line 1). A description of a genus of antagonists may be achieved by means of a recitation of a representative number of antagonists, defined by structure, falling within the scope of the genus. However, the instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of antagonists that would distinguish the claimed antagonists from other molecules that do not have the claimed biological properties. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of one specific peptide and related antibody is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of antagonists, and therefore conception is not achieved until

reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an antagonist that inhibits the interaction between MMP-9 and $\alpha 5\beta 1$ integrin wherein said antagonist is the polypeptide of SEQ ID NO:1 or the monoclonal antibody FM155, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
December 17, 2003